

With Ours best Respects



OBSERVATIONS ON THE BLOOD,
WITH REFERENCE TO ITS PECULIAR CONDITION IN THE
MORBUS BRIGHTII.

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THE examinations of diseased blood which I had an opportunity of making at Guy's Hospital during the past summer, and the results of which will be found appended to each Case as given in the present Number of the Reports, have shewn much matter of interest in their general bearings; and as it is my intention to compare these diseased conditions with the healthy standard, and moreover to enter upon observations connected with the intimate structure of the blood, I may perhaps be excused for premising my remarks by detailing a few experiments, made with a view of proving the anatomy and true mechanical relations of the blood-corpuscle. The diseased condition, to which I have above referred, interferes with many of the physical attributes of the blood; and I am therefore anxious that medical readers should be satisfied on several points relating to the physical condition of the blood in health, before venturing to draw conclusions from what has been observed in disease.

It is hoped that the experiments about to be described may shew the necessity for a correct knowledge of physical structure on the part of those who are occupied in the chemical examination of the blood; and, also, that it may appear how we occasionally possess means of proving on large masses the views to which we have been led by microscopic examination—a method of inquiry which, valuable as it certainly is, must always be received with the distrust naturally felt towards a means of investigation so tempting to the imagination, and which, it is to be feared, has already been productive of much mischief in the hands of the ingenious and unscrupulous.

A careful perusal of the various anatomical and chemical works published on the blood will shew to the reader, that the writers on both branches of science begin to be at fault at one and the same point; that being, when they treat of the colouring matter of the blood, and its true relation to the corpuscle. They know well that the blood, while circulating, is composed of blood-corpuscles, suspended in a liquor; and they describe how this liquor, when the blood is drawn, deposits fibrin, and retains its albumen, extractives, and salts in solution, forming serum: they know, too, that the fibrin adheres to the blood-corpuscles; and the two together make up the mass called crassamentum: but from this point the subject becomes confused; and the anatomist who refers to chemical works for assistance will be equally at a loss with the chemist, who contents himself with a review of the present state of microscopic science, as applied to this branch of physiology. The most recent works on the chemistry of this subject shew a complete want of information concerning the physical conditions under which the red colouring matter is placed; and the processes recommended for its extraction are very unsatisfactory to the microscopic anatomist, who, if he refer to any recent work on the chemistry of the blood, (take for instance the quarto of Lecanu,) will, from the knowledge he possesses of physical structure, be not only dissatisfied, but thoroughly convinced that such a process as that recommended for the extraction of hæmatosine can scarcely be looked upon otherwise than as a means of obtaining a red matter changed by the action of powerful re-agents, and in admixture with the various products of the action of sulphuric acid on animal membrane. Let us imagine a physiologist referring to the work above mentioned;—and how will he be assisted? The process for the extraction of hæmatosine commences as follows:—The blood, fresh drawn, is to be deprived of its fibrin by beating it with twigs while coagulating, and then sulphuric acid is to be added to the remaining red liquor until it becomes brown and nearly solid. There is no occasion to enter further on this process. I shall, I trust, be able to shew how this first step is grossly inconsistent with what we know of the physical structure of the blood. Now, if it can be proved that the red colouring

matter is contained in a vesicle, that vesicle with its inclosed coloured matter making up the blood corpuscle, we at once perceive the extreme awkwardness of this process, which, instead of first exposing the colouring matter mechanically, and then proceeding to extract it, subjects it, or rather its containing sac, to the action of a powerful re-agent; thus attacking it only after the formation of inconvenient products consequent on the destruction of an albuminous membrane by sulphuric acid; making it a difficult matter to believe that we at last obtain it in a form to exhibit the properties it possessed while circulating. Had the chemist been aware of that which I shall now notice, he would have been enabled, first to separate the blood corpuscles, then to burst them, and so obtain their coloured contents in solution for chemical examination.

In proceeding to treat of the red colouring matter as a constituent of the blood-corpuscle, I must premise that great confusion has arisen from the terms, red particle, red globule, and red corpuscle, being regarded as synonymous with hæmotosine or colouring matter; the latter expression meaning, in its correct signification, nothing more than one of the constituent parts of the red corpuscles; there being a white matter also present in those bodies, which chemists have only noticed within the last few years, and have never yet ventured to define more particularly than as the white matter of the corpuscles.

Assisted with the evidence afforded by some recent microscopic observations, I have been led to determine on a larger scale what I believe to be the true relation between the red colouring principle or hæmotosine and the white matter of the corpuscles. The microscopic experiments to which I allude* demonstrated that the red corpuscles were closed sacs, containing a fluid within them; and made it a matter of interest further to ascertain whether the fluid were red; or, on the contrary, that the corpuscle owed its colour to the redness of the enveloping membrane, the fluid within being without colour. The former of these views is certainly the

* Rees and Lane on the Structure &c. Vide Guy's Hospital Reports, No. 13.

most generally entertained by micrographers, though we find Schultzé regarding the latter as the more correct:—and it is not easy to devise means for testing the truth of either position by microscopic examination.

In considering this question, it occurred to me, that if the blood corpuscle were a closed sac, and capable of being burst by the addition of water (a point proved by the microscopic experiments above alluded to), we might, by thus treating a large quantity of collected corpuscles and bursting them, be enabled to collect the burst cases in mass at the bottom of the water, which would hold their contents in solution;—that we could thus examine their colour, and by this simple experiment set the question at rest. With this view, the serum was decanted from a specimen of coagulated blood: the clot was next carefully washed in the serum, in order to get as many red corpuscles as possible into the liquor: it was then removed, and the serum set aside to allow the red corpuscles to subside. Subsidence being complete, which occupied several hours, the supernatant serum was decanted, as nearly as possible without disturbing the deposit, and the deep-red thick mixture at bottom poured into distilled water, in order to burst the membranes of the corpuscles. This aqueous mixture was then well stirred, and set aside; when, after a few hours had elapsed, I observed a white deposit at the bottom of the containing vessel, while the supernatant liquor remained quite clear, and of a fine red colour. Now, with a previous knowledge that the blood corpuscles are burst by water, and likewise that they are sacs containing a fluid, this experiment makes it pretty certain that the containing sacs are white, and the contained liquor of a red colour.

I do not wish here to enter at length on the description of what I feel confident in my own mind should be regarded as the nucleus of the blood-corpuscle; but merely have to state, that the microscopic examination of the white precipitate to which I have above alluded has completely confirmed my former views of this question; satisfying me that the deposit is made up of burst membranes of corpuscles, and of nuclei; the latter being apparently the same structures which some writers have regarded as corpuscles deprived of their red colouring matter—a condition which, from what has

already been demonstrated concerning the corpuscle, can never occur; inasmuch as destruction of the inclosing membrane of the corpuscle is necessary before its colouring matter can be extracted: after which violence, it is obvious that any soft solid maintaining a definite form, and which can be seen and measured under the microscope, must be some constituent of original organized structure, which has now become disintegrated.

The opinion, that the membranes of the blood-corpuscles, notwithstanding their extreme tenuity, possessed in common with other animal structures the property of admitting the passage of fluids in accordance with the law of endosmose, and which was first noticed and described by Mr. Lane and myself in the *Guy's Hospital Reports*, has been, up to the present time, entirely supported by microscopic evidence. I am anxious, on the present occasion, to prove the truth of this view, by relating some experiments conducted on large quantities of blood; not only more firmly to establish a necessary premise to my conclusions, but also to shew that the correctness of opinions, the results of microscopic examination, occasionally admits of being proved by experiments conducted on masses visible to the unassisted eye. Now, if it be true that liquors pass in and out of the blood-corpuscles in proportions bearing a ratio to their specific gravities, then, if a large quantity of corpuscles be collected, we ought, by treating them with solutions of different densities, to be able to produce conditions which will differently affect their contents; the higher specific gravities taking out large proportions of those contents; the lower specific gravities removing less from within the corpuscle: and our liquors obtained after deposition has occurred ought to be differently coloured accordingly: some should be deeply tinged with red; others almost white, having, from their less-specific gravity, entered the corpuscle in large proportion, and only drawn out a very small quantity of its coloured liquor.

The results obtained from experiments conducted as above described have been in exact accordance with those microscopic views, the correctness of which they were intended to test: thus, when a quantity of corpuscles obtained by subsidence from serum were mixed with a solution of common

salt, as nearly as possible of the specific gravity of the liquor by which the corpuscle was surrounded, and consequently of the same specific gravity as the liquor within, the mixture deposited the corpuscles unaltered, and the supernatant solution was colourless, owing to the difficulty of any admixture occurring between liquors of the same specific gravity through the membrane containing the red colouring matter. When, however, a liquor of higher specific gravity was mixed with another portion of these subsided corpuscles, then the conditions were completely altered; the subsided corpuscles exhibiting a darker colour at the bottom of the vessel, owing to their aggregating more closely from being to a certain extent collapsed; and the supernatant liquor, instead of being colourless, was tinged of a deep red; the liquor of higher specific gravity having extracted a large quantity of the contents of the corpuscles. When the reverse of this experiment was performed by making the mixture with a solution of less-specific gravity than the liquor within the corpuscle, then the subsided mass was less compact, and somewhat lighter in colour, but still red; and the supernatant liquor exhibited but a feeble and scarcely perceptible tinge of pink, owing to the small quantity of colouring matter which could escape from within the corpuscles; while the liquor of less-specific gravity would enter in large proportion from without, swelling them, and thus making them occupy more room as a precipitate. It may be stated here, that a solution of any salt which does not act as a precipitant of serum, or even sugar, will serve to shew these effects; the conditions produced being then entirely governed by the specific gravity of the solutions, and in no way resulting from the chemical qualities of the salt. The next point to which I must allude, in connection with the subject of healthy blood, is the condition of the iron, and its true position in the organization of the corpuscle. It has already been proved that the red colouring matter is a fluid contained within a vesicle; which vesicle allows of the passage of fluids from without to within, and *vice versa*, according to certain fixed laws: and I shall now endeavour to shew that the iron of the blood is contained in this red liquor, and not in any other of the constituent parts of the corpuscle. If we repeat

the first experiment which I detailed, and which consisted in bursting the vesicles of a mass of corpuscles, and so destroying them by the addition of distilled-water, we can obtain a solution of their coloured contents, either by allowing the subsidence of the cases and nuclei and pouring off the clear liquor, or by performing a careful filtration through doubled blotting-paper. If the clear solution so obtained be now evaporated to dryness, I find, by incineration of the dried mass, that it contains the whole of the iron of the corpuscles; while the white matter which subsides (composed of burst cases and nuclei), if well washed from adhering colouring matter, does not yield the slightest indication of the presence of the metal. We may therefore conclude that the red liquor of the corpuscles contains the whole of the iron, and in a very soluble form.

Those who have studied the appearances put on by the blood-corpuscles, as seen under the microscope, whatever may be their opinion concerning the method of re-production, will, I am sure, allow that corpuscles of a smaller size are constantly to be detected mixed up with those of mature growth; and I have myself, on several occasions, been satisfied, by experiment, that these smaller corpuscles possess precisely the same physical attributes as the larger ones, in relation to endosmotic phenomena. Now, it must be a necessary part of the process by which these small corpuscles arrive at maturity, that iron enter within the envelope, to supply one of the constituents of the red colouring matter; and to ensure this effect, two conditions are required:— 1. A liquor containing iron in solution must be applied to the membrane of the corpuscle; and, 2. This liquor must be of a specific gravity less than that contained within the corpuscle, or it will not enter it in quantity. Both these required conditions are to be found as physico-chemical characteristics of the mixture of chyle and lymph, which enters the blood by the thoracic-duct, to which fluid all experimenters have given a lower specific gravity than the liquor sanguinis. Thus the specific gravity of the contents of the thoracic-duct in the human subject, which I lately analysed*, was 1024, while that of the liquor sanguinis may be given at about 1052, at the least.

* Vide Philosophical Transactions for 1842, Part I.

From other experiments, on the cat, the dog, and the ass, I am satisfied of the general truth of this statement. The iron which exists in the chyle is not contained in the crassamentum, which forms by coagulation; but we find it, on the contrary, as a constituent of the serum in a perfect state of solution, so that it may enter with facility through the membranes of the corpuscles: so perfect, indeed, is this solution, that, even after evaporating the chyle to dryness, we are enabled to extract the iron from the albuminous matters by digestion in water. It exists, in fact, dissolved in that constituent of the chyle which is called the aqueous extractive, and most probably in the form of lactate. Nature has, then, in this admirable manner provided for the introduction of iron into the corpuscle, by presenting it in a perfectly soluble form to the enveloping membrane, and dissolved in a liquor of a specific gravity suited to effect the necessary endosmotic actions.

Having thus shewn the reason why iron exists in the serum, and not in the crassamentum of the chyle—and also, why the contents of the thoracic duct are of less specific gravity than the liquor sanguinis—I wish to direct attention to the series of pathological phenomena which may be expected to arise when this due balance and arrangement of the physical properties of the fluids becomes destroyed, and when, by a diseased condition of longer or shorter duration, the blood so far varies from its normal standard as to present obstacles to the performance of those actions on the part of the chyle which must be considered as necessary for the preservation of animal life.

From what has been demonstrated at the commencement of this Paper, it is evident, that as the important changes of respiration occur in the colouring matter of the corpuscle, and since that colouring matter is contained within a membrane, a healthy condition of this envelope, such as admits of the transmission of liquors and gases according to certain fixed laws, is as necessary for the maintenance of life and health as is the perviousness of the larynx, trachæa, or bronchi; and any general cause acting upon the corpuscle, so as to interfere with those properties, may be expected to destroy life as rapidly as would the closure of any of the

openings communicating between the atmosphere and the internal pulmonary surface.

Again, let the blood become deranged so that its specific gravity is lessened, and we may feel assured, that if the physical qualities, more especially the specific gravity of the chyle, be not simultaneously affected, and that, too, in a due proportion, the result must be, that the red colouring matter, the great oxygenator of the blood, is no longer produced in its ordinary quantity; the ferruginous serum of the chyle not being able to enter the blood-corpuscle as in health. Again, if the degeneration above alluded to take place, we must recollect that all the solids of the body through which the blood courses are formed with pores and of material admitting of endosmotic action; and that it is impossible for the solid constituents to preserve their health if constantly acted upon by the blood at a specific gravity of 1030 to 36, instead of 1052 to 57; the equilibrium of health being no longer preserved, and the watery blood inducing a like condition in the other solids. In throwing out these suggestions, I am prompted by a desire to draw the attention of the Profession to the great importance of the study of endosmotic action, as applied to pathology; many of the phenomena of the *Morbus Brightii* being apparently attributable to a condition of blood such as I have above noticed.

On examining the Table (which will be found at the end of this communication, and consulting the Cases with chemical notices appended, the following will appear the prominent features to which attention should be more especially directed:—1. The excessive quantity of water in the blood. 2. The existence in the blood of one of the ingredients of the urine. 3. The existence of the same ingredient of the urine in the milk, and also in the fluids effused into various serous cavities. 4. The absence or deficiency in the urine of one or more of the natural ingredients of the excretion. 5. The general watery condition of the urine. 6. The existence of albumen in the urine.

When considering the part taken by the blood in producing the *Morbus Brightii*, it must not be too rapidly concluded that those changes which are observed in more advanced stages of the disease are identical in kind, and differing only in degree from those occurring at the com-

mencement of a severe and fatal case; or that they are the cause of the symptoms, terminating in perfect recovery, which we so often observe in mild cases of anasarca with coagulable urine following scarlet-fever. The diseased conditions of the blood noticed in the Table may, however, I think, well be considered the cause of the train of secondary symptoms attendant on the *Morbus Brightii*; and the first morbid condition induced may be (as has been rendered more than probable by the late ingenious researches of Mr. Robinson) simply a congested state of the kidney—a mechanical derangement of circulation—giving rise to a filtration of the albuminous matters of the blood into the urine; a drain on the system which, by impoverishing the vital fluid, may, in its turn, make the blood a cause of further symptoms, such as would never have developed themselves had not the primary disease been manifest. All, indeed, that we know of the history of this degeneration of the kidney, the mild character of some of the cases, and the facility with which the disease, as following scarlatina, admits of cure—tends to shew, that in the commencement the blood may be perfectly healthy, and the albumen in the urine the result of congestion by blood in its normal state.

There is, however, a fact in the history of this affection which does not render it altogether improbable that the presence of an excess of water in the blood may, in some cases at least, assist in bringing about the effusion of serum into the urine. I allude to the frequency of a dry skin, observed in some early cases. The probability that such a state of the cutaneous surface acts as a cause is considerably increased by the tendency to this kind of dropsy after the cutaneous surface has been involved by an attack of scarlatina, which produces a form of *Morbus Brightii*, for the most part easily admitting of cure. The difficulties which must necessarily occur in freeing the blood of water when the action of the skin is lessened or entirely stopped must be considered as very great, when we remember the large quantities of fluid daily given off from the cutaneous surface, and the small excess only in the quantity of urine characterizing any form of *Morbus Brightii*;—the greater number of cases, indeed, passing less than the natural quantity. In making the above

suggestion, I in no way wish it to be inferred as my belief that congestion alone is incapable of producing coagulable urine; indeed, as stated before, direct experiment has shewn to the contrary: but it is certain that the tendency to the entrance of albumen into the urine will be increased by dilution of the blood; and we frequently observe a condition occurring, at the very outset of the disease, favourable to the production of this form of deterioration in the circulating fluid.

The secondary symptoms of the *Morbus Brightii*—such as effusion into the large serous cavities or the ventricles of the brain, general cellular effusion, and the peculiar anæmic appearance which, even when no swelling of the face exists, is frequently so characteristic as to attract the practised eye—are easily explicable as results, when once we are acquainted with the watery state of the blood, and the physiological conditions necessary to preserve the integrity of the blood-corpuscle. The obvious mechanical assistance which an excess of water must afford for the production of general effusion needs no comment; but it may be a matter of difficulty to some, to explain how it is that the blood loses its red colouring matter; and which, to be clearly understood, requires an insight into the more minute changes occurring in the fluid, as a result of its aqueous condition. I have before shewn, that if the chyle does not accommodate itself in relative specific gravity to the blood, the necessary endosmotic actions cannot take place between the two fluids; and we may consequently expect difficulty in the production and growth of the red corpuscles, inasmuch as the iron cannot be supplied for the formation of colouring matter, the ferruginous serum of the chyle no longer entering through the membrane of the blood corpuscle in virtue of its less specific gravity: and I think it may be maintained as the correct view, that this is really the cause of that great diminution in the proportion of colouring matter observed in the blood of patients affected with the advanced stage of the *Morbus Brightii*. This diminution in the proportion of red corpuscles does not occur in early cases of the disease, however confirmed in character: an example of which may be seen by referring to the history of George Moore, 14 Job Ward, a mild case, probably admitting of permanent cure, in which the blood contained more

than the normal proportion of fibrin and corpuscles; the albumen being very deficient, the serum light, and the water of the blood in about its natural quantity. We here see the first effects of the disease—the blood becoming deprived of its albuminous ingredients; a condition which, if it continue, will produce the next change; viz. a deterioration in the specific gravity of the contents of the corpuscle, owing to the liquor sanguinis becoming lighter, and endosmosing that structure: this state again soon succeeded by a lessening of the number of red corpuscles, attributable to the requisite actions no longer taking place on the part of the chyle, in the manner described in a former part of this Paper. The occurrence of inflammation in this disease, as will be seen by the analysis of the blood in the case of Holywell, produces the usual increase in the quantity of fibrin in the blood: this, however, did not happen to any considerable degree in the case of Charles Scott.

The existence of urea in the blood, and effusions obtained from the patients in the male and female wards, and also in the milk of a patient in Lydia Ward, has been satisfactorily proved: indeed, I have never yet failed to obtain it in sufficient quantity to shew its physical and chemical characters. The process employed for the blood and effusions is described in the Tenth Number of the Guy's Hospital Reports; and I find it to be, with slight variation, the best calculated for extracting urea from the milk. For this latter purpose the milk must be evaporated to dryness; and then several times digested with æther, which will extract the whole of the fatty matters, together with the urea; the latter being easily separable by heating the dry ethereal extract with water, and stirring it well during the digestion. After this process the urea exists dissolved in the water, which may be poured off from under the fatty matter, the latter having caked above the liquor on cooling.

As regards the urine in the Morbus Brightii, the deficiency of urea, and occasional deficiency or absence of lithic acid, its watery condition, and the presence of albumen, the two former states may in all probability be attributed to the derangement of the kidney alone; and the two latter, in some measure, to the condition of the blood. I am not aware that

the total absence of lithic acid from the urine has been before observed. That such was the case, however, was proved by rigorous chemical and microscopical examination; the former consisting in evaporating the urine to a small quantity, adding muriatic acid, and carefully analysing any precipitate so obtained.

Albuminous urine, when viewed under the microscope, exhibits granules and corpuscles of varying form and size; the larger of which might be mistaken for the pus-globule by careless or inexperienced observers. The true source, however, of these bodies is, in all probability, the serum of the blood, which I find deposits analogous granules and corpuscles when diluted by a liquor of light specific gravity; which may easily be proved by pouring distilled water on serum, and submitting to the microscope the precipitate which collects after a few hours have elapsed. In other respects, coagulable urine presents the ordinary appearances under the microscope; the solid ingredients or crystallizable products exhibiting, when present, their usual characteristics. Some specimens shew very well the large form of granulated mucous globule known as the secretion of the prostate.

In concluding this communication, I cannot help expressing a hope that the many points of interest which the study of the *Morbus Brightii* affords may receive the early attention of physiologists; believing, as I do, that careful observation of the phænomena occurring in this disease must eventually throw much light both on the true nature of the blood-corpuscle and the all-important offices of the function of respiration.

TABLE of RESULTS of Examinations of BLOOD and URINE in MORBUS BRIGHT

Whence obtained.	Blood: Composition in 1000 parts.	Urine.	REMARKS.
WILLIAM CURTAIN, 22 Job Ward.	Water . . . 853·11 Solid matters } of serum } 81·28 Fibrin and } corpuscles } 65·61 Serum in 1000 parts: Albumen . . . 68·5 Urea 0·5 Alkaline salts, 6·0	18 fluid oz. were passed in 24 hours, each oz. yielding 5·2 gr. of albumen (dry): sp. gr. of urine 1015: urea 8·1 per 1000. No lithic acid could be detected in this urine, in any form, either combined or free.	Specific gravity serum was 1023: not milky. The blood very slightly buffed.
CHARLES SCOTT, 3 Job Ward.	Water . . . 835·85 Solid matters } of serum } 82·54 Fibrin and } corpuscles } 81·61	32 fluid oz. passed in 24 hours: sp. gr. of urine 1011, each ounce containing 2·05 gr. of albumen. Lithic acid present, in small proportion.	Blood buffed and cloudy.
JAMES BACK, 2 Job Ward. Disease complicated with Phthisis.	Water . . . 828·92 Solid matters } of serum } 76·98 Fibrin and } corpuscles } 94·10	Containing 7·75 gr. of albumen in each oz.: urea 8·73 per 1000.	Serum contained parts of albumen in 1000.
GEORGE HOLYWELL, 4 Job Ward. Disease accompanied with effusion into the Pleura.	Water . . . 777·06 Solid matters } of serum } 71·14 Fibrin and } corpuscles } 151·80	For particulars, see the Cases in present Number.	Blood buffed and cloudy. sp. gr. of the serum containing in 1000 albumen 64 and solid parts. Urea detected but not estimated.
GEORGE MOORE, 14 Job Ward.	Water . . . 782·86 Solid matters } of serum } 73·14 Fibrin and } corpuscles } 144·00	Serum of sp. gr. 1012, containing in 1000 albumen 72, and urea 8·73 parts.
ELIZABETH McINNES, 5 Lydia Ward.	Water . . . 805·71 Solid matters } of serum } 85·56 Fibrin and } corpuscles } 108·73	Sp. gr. 1012, containing 1·5 gr. of albumen in each oz., and no trace of lithic acid in any form.	Serum of sp. gr. 1012, containing in 1000 alkaline salts 7·7 parts of serum.
From a healthy individual, for comparison.	Water . . . 792·20 Solid matters } of serum } 87·85 Fibrin and } corpuscles } 119·95	Sp. gr. 1022: urea 30·1, and lithic acid 1·0 parts per 1000. No trace of albumen.	Serum of sp. gr. 1022, containing in 1000 albumen . . . 77 alkaline salts in 1000 parts.

